8. Bartlett JG: Antibiotic-associated diarrhea. Clin Infect Dis 1992; 15:573-581

9. Firestein GS, Zvaifler NJ: Reactive arthritis. Annu Rev Med 1987; 38:351-360

10. Keat A: Reiter's syndrome and reactive arthritis in perspective. N Engl J Med 1983; 309:1606-1615

11. Arnett FC: Seronegative spondyloarthropathies. Bull Rheum Dis 1987; 37:1-12

12. Inman RD: Arthritis and enteritis—An interface of protean manifestations (Editorial). J Rheumatol 1987; 14:406-410

13. Gran JT, Husby G: Joint manifestations in gastrointestinal diseases—2. Whipple's disease, enteric infections, intestinal bypass operations, gluten-sensitive enteropathy, pseudomembranous colitis and collagenous colitis. Dig Dis 1992; 10:295-312

14. Reiter H: Ueber eine bisher unerkannte Spirochateninfection (Spirochaetosis Arthritica). Dtsch Med Wochenschr 1916; 42:1535-1536

15. Rollins DE, Moeller D: Acute migratory polyarthritis associated with antibiotic-induced pseudomembranous colitis. Am J Gastroenterol 1976; 65:353-356

16. Fox R, Calin A, Gerber RC, Gibson D: The chronicity of symptoms and disability in Reiter's syndrome—An analysis of 131 consecutive patients. Ann Intern Med 1979; 91:190-193

Vasculitis Possibly Confined to the Small and Large Intestine

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VASCULITIS OF THE GASTROINTESTINAL TRACT is an uncommon disorder and typically accompanies systemic manifestations of a vasculitic process.[1] We report a case of isolated gastrointestinal vasculitis affecting both the small and large intestine.

Report of a Case

The patient, a 73-year-old woman with a history of controlled hypertension, deep venous thrombosis of the calf in 1982, and a minor cerebrovascular accident in 1976, presented to her primary physician six months before admission with progressive, diffuse, crampy abdominal pain exacerbated by eating and associated with weight loss. Three months before admission she had bloody diarrhea, and a flexible sigmoidoscopy revealed diffuse redness and friability in the rectosigmoid area. Biopsies revealed nonspecific acute and chronic mucosal inflammation. A computed tomographic scan of the abdomen, air-contrast barium enema, and an esophagogastroduodenoscopy were normal. Abdominal ultrasonography was unremarkable, other than for the presence of gallstones. Laboratory data included a hemoglobin level of 80 grams per liter (8 grams per dl), with a mean cellular volume of 73 fl, and liver function test values were normal. The patient was treated with metronidazole for presumed infectious colitis, without benefit. She also received ferrous sulfate, and her hemoglobin value increased to 137 grams per liter (13.7 grams per dl) over the next six weeks. A month before admission, the patient continued to have abdominal pain and hematochezia, and her hemoglobin level had dropped to 85 grams per liter (8.5 grams per dl).

The patient was admitted to a community hospital where a flexible sigmoidoscopy revealed rectosigmoid friability without ulceration. A presumptive diagnosis of ulcerative colitis was made. Treatment with sulfasalazine (Azulfidine) and methylprednisolone sodium succinate (Solu-Medrol), 40 mg a day intravenously, was begun. Two days later an acute abdomen developed, and the patient's leukocyte count was noted to be 40×10^9 per liter (40,000 cells per mm^3). The patient was taken to the operating room where extensive small bowel necrosis with gangrene was found. The small bowel was resected from the midjejunum to the ileocecal valve, and a right hemicolectomy was performed because the colonic serosa appeared dusky. Mesenteric arterial pulsations were thought to be within normal limits, mesenteric veins did not appear unusual, and a jejunocolostomy was done. Microscopic review of the specimens showed transmural necrosis of the bowel, consistent with ischemic necrosis, and the presence of thrombi in small mesenteric veins.

After the operation, the patient had diarrhea and recurrent hematochezia. Esophagogastroduodenoscopy was within normal limits, and a flexible sigmoidoscopy revealed mild erythema and edema to 50 cm without ulceration or friability. This was thought to be an improvement from the previous examination, and her steroid regimen was tapered off. Persistent hematochezia requiring the transfusion of 10 units of packed erythrocytes prompted a mesenteric angiogram, which revealed grossly normal superior and inferior mesenteric arteries without aneurysms or atherosclerotic disease. A blush without extravasation was seen in the midjejunum, consistent with an arteriovenous malformation.

Two weeks later the patient was transferred to the University of California Center for Health Sciences at Los Angeles (UCLA) for further management. At that time she had mild abdominal pain. The patient had no visible skin or joint lesions, and her stools were brown and positive for occult blood. Push enteroscopy with a Pentax 3400 colonoscope revealed three nonbleeding arteriovenous malformations in the antrum, proximal duodenum, and proximal jejunum, respectively, which were treated with bipolar electrocauterization. Colonoscopy to the surgical anastomosis revealed swollen mucosal folds with a loss of the normal vascular pattern throughout. There were ulcerations in the rectum and severe nodularity with punched-out ulcerations in the mid-sigmoid colon (Figure 1). The anastomotic site was deformed and friable and could not be traversed. Endoscopic biopsies from the involved colon again revealed acute and chronic mucosal inflammation without specific features.

Histology slides and gross specimens from the previous small and large bowel resection were then re-

(Freilich BL, Bernstein CN: Vasculitis possibly confined to the small and large intestine. West J Med 1995; 162:63-65)

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Dr Bernstein's work is supported in part by the Blinder Foundation for Crohn's Disease Research.

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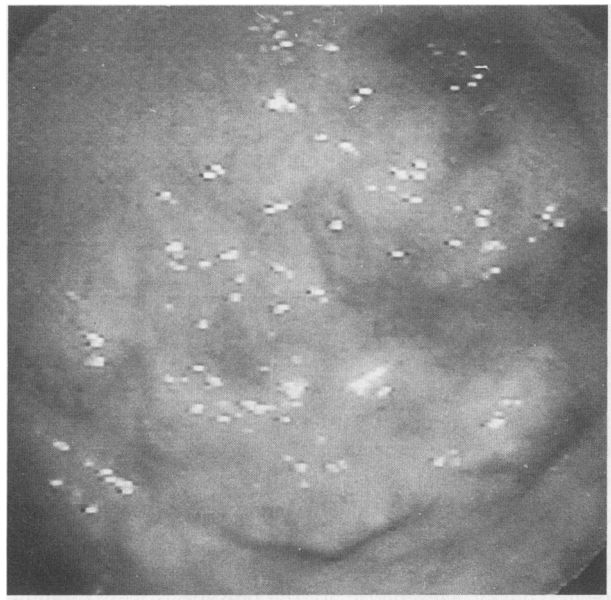

Figure 1.—Endoscopy of the sigmoid colon reveals multiple punched-out ulcers and underlying nodular edematous mucosa.

viewed at UCLA. The small intestine showed transmural ischemic infarction with ulceration and acute inflammation throughout the bowel wall (Figure 2). In addition, sections of the mesentery revealed acute vasculitis of many medium-sized arteries in areas remote from the bowel necrosis and inflammation. The vasculitis was characterized by a neutrophilic infiltrate of the vessel walls and disruption of the internal elastic lamina with fibrinoid necrosis and thrombosis (Figure 3). No giant cells or granulomas were seen.

Echocardiogram showed no evidence of thrombus and a normal myocardium. Her urinary sediment was bland without casts or erythrocytes, and a 24-hour urine collection revealed a creatinine clearance of 1.12 ml per second

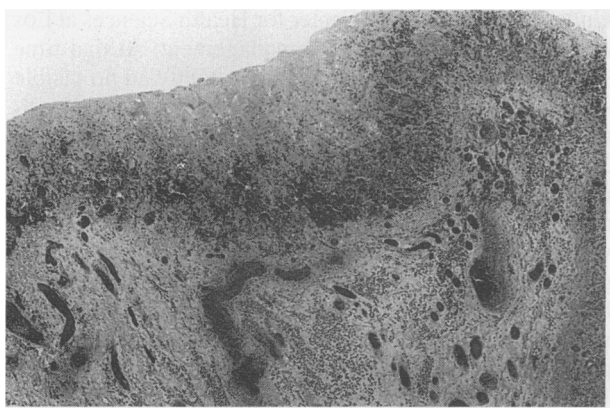

Figure 2.—A low-power view of the small bowel wall shows necrosis of the mucosa and submucosa. Many small submucosal vessels are dilated and congested, and an acute and chronic inflammatory infiltrate is present throughout the bowel wall (hematoxylin and eosin stain, original magnification × 25).

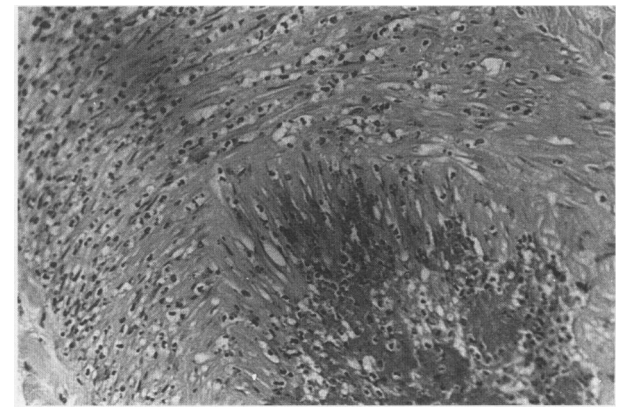

Figure 3.—A high-power view of the small bowel wall shows a medium-sized artery in the small bowel mesentery. All levels of the artery wall are infiltrated by acute inflammatory cells. The intima shows fibrinoid necrosis, and the vessel is thrombosed (hematoxylin and eosin stain, original magnification × 200).

(67 ml per minute) and a protein concentration of 0.14 grams per day (135 mg per 24 hours). Serologic examination revealed normal blood urea nitrogen and serum creatinine levels; negative titers for rheumatoid factor, antinuclear antigen, and antineutrophilic cytoplasmic antibody; a negative Raji assay; and normal complement levels. Antithrombin III and protein C and S levels were normal. A high titer of the lupus anticoagulant was found, although assay for anticardiolipin antibody was negative.

The patient was diagnosed with vasculitis of the small intestine and colon, and intravenous therapy with methylprednisolone, 50 mg per day, was begun. Her previous gastrointestinal bleeding was ascribed to diffuse colonic oozing due to severe ischemic colitis and did not recur while she was at UCLA. She was maintained on total parenteral nutrition and enteric supplements. Her diarrhea persisted and was thought to be predominantly due to a short gut syndrome.

Discussion

This case is one of isolated small and large intestine vasculitis. It is unique because it is the first case of isolated intestinal vasculitis reported to involve both the small and large intestine and is only the fifth case in the literature of isolated intestinal vasculitis without systemic signs of vasculitis.[2-5] This patient more likely had systemic vasculitis (with a positive lupus anticoagulant) with isolated intestinal manifestations, rather than primary intestinal vasculitis. Other cases of isolated intestinal vasculitis have had pathologic findings consistent with more diffuse processes. A case of isolated small intestinal vasculitis leading to perforation and death was reported, with autopsy findings consistent with polyarteritis nodosa.[2] In another case, isolated giant cell arteritis occurred, leading to intestinal perforation,[3] and a case of isolated ileal vasculitis as a paraneoplastic syndrome to a recurrent breast adenocarcinoma was also reported.[4] The disease in these three cases was limited to the small intestine. A case of isolated vasculitis was limited to the right colon, with pathologic

findings consistent with granulomatous inflammation and necrotizing vasculitis, possibly polyarteritis nodosa, selectively involving branches of the right colic artery.[5]

Gastrointestinal vasculitis is a fairly uncommon disorder and often difficult to diagnose. Patients frequently present with bloody diarrhea and abdominal pain, and the disease may ultimately lead to intestinal ischemia and perforation.[1] Ischemia from vasculitis is clinically similar to atherosclerotic and embolic disease[6] and can be confused with Crohn's disease.[5]

One group of investigators has suggested that careful histologic examination of the intestinal mucosa in Crohn's disease may reveal a granulomatous vasculitis,[7] and there are reports of cutaneous vasculitis[8,9] and the presence of anticardiolipin antibodies[10,11] in patients with Crohn's disease. Our patient did not have granulomatous vasculitis, and vasculitic arteries were often present in areas remote from areas of inflammation (which is unusual in Crohn's disease). Furthermore, extensive intestinal infarction is not a feature of Crohn's disease. Another of the idiopathic forms of inflammatory bowel disease, ulcerative colitis, is a disorder confined to the mucosa of the large intestine. There are reports of occasional instances of systemic vasculitis in association with ulcerative colitis,[9] including cutaneous polyarteritis nodosa,[12] systemic lupus erythematosus,[13] and Wegener's granulomatosis.[14] Ulcerative colitis can be associated with the presence of an antineutrophilic cytoplasmic antibody (that stains in a perinuclear pattern on immunofluorescence, as opposed to the more typical cytoplasmic granular pattern in Wegener's granulomatosis) in 70% of patients.[15] Our patient's disease was certainly not ulcerative colitis, as it extended to the small intestine and was associated with transmural inflammation.

Gastrointestinal vasculitis is almost always accompanied by systemic manifestations of disease. The largest series of such patients was reported in 1983, wherein 18 of 65 patients with systemic vasculitis had disease affecting the gastrointestinal tract.[1] Most of these patients had polyarteritis nodosa or microscopic polyarteritis (disease affecting small vessels with normal angiograms). Wegener's granulomatosis and the Churg-Strauss syndrome were found less commonly. Of the 18 patients with gastrointestinal manifestations, 17 had focal glomerulonephritis on renal biopsy, and all had clinical signs of glomerulonephritis. Necrotizing vasculitis was found on skin biopsy in 6 of 18 patients with purpuric lesions. Other connective tissue diseases more commonly associated with gastrointestinal vasculitis include systemic lupus erythematosus,[17] rheumatoid arthritis, and hypersensitivity vasculitides.[18]

Angiographic findings are generally remarkable only in cases of polyarteritis nodosa where aneurysms are found in medium-sized mesenteric vessels.[1] Endoscopic diagnosis is also challenging, as routine luminal biopsy specimens through flexible endoscopes rarely show the diagnostic lesions. Deep rectal biopsies through rigid proctoscopes, however, may have a slightly higher yield.[16] Often the diagnosis is a clinical one, with intestinal disease accompanying other systemic signs of vasculitis.

Our case was also complicated by the presence of mesenteric vein thromboses. These thrombi were likely due to intestinal vasculitis and gangrene, as they were not organized thrombi and, therefore, not chronic. Primary thrombus due to the lupus anticoagulant cannot be ruled out, however, especially in light of the patient's history of previous thrombotic events. The presence of the lupus anticoagulant may indicate that the patient had a truly systemic vasculitis, but presented without nongastrointestinal manifestations. There have also been reports of necrotizing vasculitis involving the mesenteric veins of patients with primary mesenteric vein thrombosis.[19] None of these patients had evidence of arterial vasculitis, as did our patient.

Intestinal ischemia with perforation or gangrene is an abdominal catastrophe with many causes. Vasculitis can certainly be one such cause, albeit rare. Our case reinforces that gastrointestinal vasculitis may present without systemic manifestations of vasculitic disease and may affect both the colon and small intestine.

Acknowledgment

Marie Robert, MD, Department of Pathology, UCLA, assisted with the histopathology in this case.

REFERENCES

1. Camilleri M, Pusey CD, Chadwick VS, Rees AJ: Gastrointestinal manifestations of systemic vasculitis. Q J Med 1983; 52(206):141-149

2. Gleeson FV, Tidbury PJ: Small bowel vasculitis. Br J Radiol 1991; 64:959-960

3. Smith JA, O'Sullivan M, Gough J, Williams BD: Small-intestinal perforation secondary to localized giant-cell arteritis of the mesenteric vessels. Br J Rheumatol 1988; 27:236-238

4. Sanchez-Guerrero J, Gutiérrez-Ureña S, Vidaller A, Reyes E, Iglesias A, Alarcón-Segovia D: Vasculitis as a paraneoplastic syndrome—Report of 11 cases and review of the literature. J Rheumatol 1990; 17:1458-1462

5. Kalla AH, Lee KU, Voss EC Jr: The dilemma of colonic vasculitis: A report of a unique case. Dis Colon Rectum 1980; 23:590-596

6. Grendell J, Ockner R: Vascular diseases of the bowel, *In* Sleisenger M, Fordtran R (Eds): Gastrointestinal Disease. Philadelphia, Pa, WB Saunders, 1989, pp 1903-1932

7. Wakefield AJ, Sankey EA, Dhillon AP, et al: Granulomatous vasculitis in Crohn's disease. Gastroenterology 1991; 100:1279-1287 [erratum published in Gastroenterology 1991; 101:595]

8. Gudbjörnsson B, Hällgren R: Cutaneous polyarteritis nodosa associated with Crohn's disease: Report and review of the literature. J Rheumatol 1990; 17:386-390

9. Lie JT: Vasculitis and the gut: Unwitting partners or strange bedfellows (Editorial). J Rheumatol 1991; 18:647-649

10. Vianna JL, D'Cruz DP, Khamashta MA, Asherson RA, Hughes GR: Anticardiolipin antibodies in a patient with Crohn's disease and thrombosis. Clin Exp Rheumatol 1992; 10:165-168

11. Greenfield SM, Teare JP, Whitehead MW, Thompson RP: Amaurosis fugax, Crohn's disease and the anticardiolipin antibody. Lupus 1993; 2:271-273

12. Chiu G, Rajapakse CN: Cutaneous polyarteritis nodosa and ulcerative colitis. J Rheumatol 1991; 18:769-770

13. Font J, Bosch X, Ferrer J, Pérez-Villa F, Ingelmo M: Systemic lupus erythematosus and ulcerative colitis (Letter). Lancet 1988; 1:770

14. Kedziora JA, Wolff M, Chang J: Limited form of Wegener's granulomatosis in ulcerative colitis. Am J Roentgenol 1975; 125:127-133

15. Shanahan F: The role of autoantibodies and autoimmunity in chronic inflammatory disorders of the gut. Curr Opin Immunol 1992; 8:988-992

16. Tribe CR, Scott DG, Bacon PA: Rectal biopsy in the diagnosis of systemic vasculitis. J Clin Pathol 1981; 34:843-850

17. Dubois EL, Tuffanelli D: Clinical manifestations of systemic lupus erythematosus: Computer analysis of 520 cases. JAMA 1964; 190:104-111

18. Fauci AS, Haynes B, Katz P: NIH Conference: The spectrum of vasculitis—Clinical, pathologic, immunologic and therapeutic considerations. Ann Intern Med 1978; 89(pt1):660-676

19. Van Way C, Brockman S, Rosenfeld L: Spontaneous thrombosis of the mesenteric veins. Ann Surg 1971; 173:561-568